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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,212	12/04/2001	Stephen D. Gillies	LEX-002C1	6802
21323	7590	01/14/2004	EXAMINER	
TESTA, HURWITZ & THIBEAULT, LLP HIGH STREET TOWER 125 HIGH STREET BOSTON, MA 02110			MERTZ, PREMA MARIA	
		ART UNIT	PAPER NUMBER	
		1646	11	
DATE MAILED: 01/14/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	10/005,212	GILLIES ET AL.
	<b>Examiner</b>	<b>Art Unit</b>

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 12/4/03.

2a) This action is FINAL.                    2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-3 and 23 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-3 and 23 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. §§ 119 and 120

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) All b) Some \* c) None of:  
1. Certified copies of the priority documents have been received.  
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

13) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) The translation of the foreign language provisional application has been received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

#### Attachment(s)

1) Notice of References Cited (PTO-892)                    4) Interview Summary (PTO-413) Paper No(s). 8.

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)                    5) Notice of Informal Patent Application (PTO-152)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8,10.                    6) Other:

## **DETAILED ACTION**

1. The amendment submitted in Paper No. 7 (3/10/03) has been entered. Claims 1-3, 23, are pending and under consideration by the Examiner.

### ***Claim rejections-35 USC § 102***

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 23, are rejected under 35 U.S.C. 103(a) as being unpatentable over Trinchieri et al. (U.S. Patent No. 5,457,038) in view of WO 97/20062.

Trinchieri et al. disclose the nucleic acid and corresponding amino acid sequence of the heterodimeric cytokine IL-12 (see abstract; Figures 1-2; column 4, lines 7-30) and also teaches that induced modifications to IL-12 to enhance its half-life (column 14, lines 41-51) but does not teach chimeric proteins comprising the first subunit of IL-12 bonded

to the IgG heavy chain molecule and a second subunit of IL-12 bonded to the IgG heavy chain molecule which increases its circulating half-life.

WO 97/20062 teaches a chimeric protein comprising IL-12 p40 subunit covalently linked to an enzymatically inactive polypeptide including the IgG heavy chain which lacks the IgG variable which is capable of extending the *in vivo* half-life of the fusion polypeptide relative to the native IL-12 p40 subunit (see page 4, line 1-6; abstract; page 1, lines 26-32; page 7, lines 13-16). The reference also teaches expression of the fusion polypeptide by transfection of a plasmid termed “p40/γ1 3/31” into cultured host cells.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art to modify the p35 and p40 subunits of IL-12 polypeptide of Trinchieri et al. by incorporating the immunoglobulin heavy chain linked by a peptide bond to each of p35 and p40 as taught by WO 97/20062, to obtain the known functions and advantages of IL-12 as per the teachings of Trinchieri et al. Cytokines such as IL-12 are well-known in the art as having a short half-life. One would have been motivated to use a chimeric protein comprising the p35 subunit of IL-12 and IgG heavy chain and the p35 subunit of IL-12 and IgG heavy chain to decrease its clearance rate *in vivo* and also since the chimeric protein would have greater biological activity than the same amount of IL-12 alone. Therefore, lower doses of IL-12 could be used therapeutically. Fusing each of the IL-12 subunits to a long-lived molecule like IgG heavy chain, would increase the stability of a rapidly cleared molecule like IL-12 and this limitation would be an inherent property of the chimeric molecule. Therefore, it would have been obvious to fuse each of the IL-12

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subunits to a long-lived molecule like IgG heavy chain, a long-lived molecule well known in the art as able to increase the stability of rapidly cleared molecules.

***Conclusion***

No claims are allowed.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (703) 308-4229. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (703) 746-5300.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

*Prema Mertz*  
Prema Mertz Ph.D.  
Primary Examiner  
Art Unit 1646  
November 25, 2002